

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 35-59, 61, 81-84, 86-100, 102-118, 120-149, 151-153, 155-166, 168-169, 176-189, 191-202, 204-209, 211-222, 224-269 and 272-286 are pending in the application, with claims 35, 81, 96, 114, 132, 152, 169, 186, 205, 225, 242, 257 and 272 being the independent claims. Claims 35-52, 54-59, 61, 81-84, 86-89, 91-99, 102, 105, 107-113, 115-117, 120-123, 125-149, 151, 153, 155-159, 161-166, 168-169, 176-179, 181-189, 192-195, 197-202, 204-209, 212-215, 217-222 and 224 are allowed. Claims 60, 79, 150, 167, 203, 223 and 270-271 are sought to be canceled without prejudice to or disclaimer of the subject matter therein. Claims 60, 79, 150, 167, 203 and 223 were the subject of a restriction requirement issued by the Examiner and have been withdrawn from consideration by the Examiner. Applicants retain the right to pursue the subject matter of these canceled claims in related applications. Claims 100, 118, 191, 211, 273-275, 279-280, 282 and 286 have been amended to more clearly and precisely define Applicants' claimed invention. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Disposition of Claims 257-269

Applicants note that the disposition of claims 257-269 (other than that they are pending) was not indicated by the Examiner in the Office Action dated November 6, 2000. Applicants respectfully request that the Examiner consider these claims and notify Applicants of their status.

Claim Objections

The Examiner has objected to claim 279 under 37 C.F.R. § 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. (Paper No. 17, page 3.) The Examiner has noted that it appears that claim 279 was intended to depend from claim 270 instead of claim 170.

Applicants thank the Examiner for pointing out this typographical error. Applicants note that claim 270 has been canceled. Claim 279 has been amended herein so that it depends from claim 272, which has been rewritten in independent form. The amendment puts claim 279 in proper dependent form. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the objection to claim 279 and the associated dependent claims.

Interpretation of Claim 270 and Rejection Under 35 U.S.C. 112, Second Paragraph

The Examiner has expressed confusion about the proper interpretation of claim 270. As noted above, claim 270 has been canceled. Accordingly, the Examiner's rejection is rendered moot and Applicants respectfully request that the Examiner withdraw the rejection.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 100, 114, 118, 152, 191, 211, 273 and 274 under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner has stated that it is "unclear what is meant by 'a polypeptide fragment which is capable of functioning as part of a mature DR5 polypeptide to induce apoptosis.'" (Paper No. 17, page 4.)

Initially, Applicants note that claims 114 and 152 do not recite the language in which the Examiner objects. Thus, the Applicants believe that claims 114 and 152 were erroneously rejected

by the Examiner. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Claims 100, 118, 155, 191, 211 and 274 recite the language objected to by the Examiner. Solely to advance prosecution and not in acquiescence to the Examiner's rejection, Applicants have amended claims 100, 118, 155, 191, 211 and 274. These claims are now directed to a "polypeptide fragment which is capable of functioning as a functional domain within a mature DR5 polypeptide to induce apoptosis." Applicants believe the amendment makes clear what Applicants consider to be the claimed invention. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

The Examiner has also rejected claim 273 under 35 U.S.C. § 112, second paragraph, as indefinite because it allegedly is unclear what is meant by the "a polypeptide fragment which is capable of functioning as part of a DR5 extracellular domain to bind TRAIL." (Paper No. 17, page 4.) Solely to advance prosecution and not in acquiescence to the Examiner's rejection, Applicants have amended claim 273 to recite a "polypeptide fragment capable of functioning as a functional domain within a mature DR5 polypeptide to bind TRAIL." Applicants believe the amendment makes clear what Applicants consider to be the claimed invention. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

The Examiner has rejected claims 53, 90, 106, 124, 143, 160, 180, 196, 216, 234, 251, 264, and 279 as allegedly being indefinite because the claims are "drawn to [a method for] producing a vector, yet the starting material is a vector." (Paper No. 17, page 4.) The Examiner has asserted that "[t]his method is then circular and does not produce anything." (*Id.*) Applicants respectfully disagree.

The term "vector" as used in the art refers to a carrier of nucleic acids, both in the case where the vector actually is associated with a nucleic acid insert and in the case where the vector is not

associated with a nucleic acid insert. In the instant case, the vector produced by the method of the claims would be different than the vector used as the starting material because the vector produced would comprise an isolated polynucleotide of the claims. Thus, the starting material and the product are different. This distinction would be immediately apparent to one of ordinary skill in the art.

The purpose of the requirement for definiteness is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent and to provide a clear measure of what applicants regard as the invention so that it can be determined whether the claimed invention meets all the criteria for patentability and whether the specification meets the criteria of 35 U.S.C. § 112, first paragraph. (M.P.E.P. § 2173.) Applicants assert that the instant claims meet this purpose. It would be plain to one of ordinary skill in the art that the vector produced by the method of the claims is distinct from the vector as the starting material. Thus, Applicants submit that the claims are not indefinite. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claim 286 under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not enable any person skilled in the art to which it pertains, or with it is most nearly connected, to use the invention commensurate in scope with these claims. (Paper No. 17, page 5.) Specifically, the Examiner has stated that "the specification, while being enabling for a method of producing a polypeptide that is at least 95% identical to 50 contiguous amino acids within amino acids 1-360 of SEQ ID NO:2 wherein said polypeptide is specifically bound by an antibody that also specifically binds the corresponding region of said 50 contiguous amino acids of SEQ ID NO:2, *does not* reasonably provide enablement for a polypeptide that cannot be bound by such an antibody." (*Id.* at pages 4-5.) (Emphasis added.) Solely to advance prosecution and not in

acquiescence to the Examiner's rejection, Applicants have amended claim 286 so that the claimed method produces a polypeptide capable of binding an antibody with specificity for a polypeptide consisting of amino acids 1-360 of SEQ ID NO: 2. Based on these remarks, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Rejections under 35 U.S.C. § 102

The Examiner has rejected claims 225, 226, 230-231, 234-240, 242-244, 247, 248, 251-255, 270-271, 273-276 and 279-285 under 35 U.S.C. § 102(a) as allegedly being anticipated by GenBank Accession No. AA223122. (Paper No. 17, page 5.) The Examiner has stated that:

GenBank Accession No. AA223122 teaches a polypeptide that is 97% identical over nucleotides 236-698 of SEQ ID NO: 1 of the instant specification. This region comprises the nucleic acid capable of encoding a contiguous stretch of 138 amino acids at least 97% identical to the corresponding stretch of SEQ ID NO:2 of the instant specification, which is encoded by a nucleotide beginning at about position 282 of SEQ ID NO: 1 for the mature polypeptide.

(Paper No. 17, page 6.) (Citation omitted.)

In order to advance prosecution, Applicants have canceled claims 270-271. Accordingly, the Examiner's rejection of these claims is rendered moot and Applicants respectfully request that the Examiner withdraw the rejection.

After cancellation of claims 270-271, the claims at issue in the instant rejection are claims 225, 226, 230-231, 234-240, 242-244, 247, 248, and 251-255.¹ These claims are directed to isolated polynucleotides comprising a nucleic acid which encodes a polypeptide with identity to amino acids 1 to 133 of SEQ ID NO: 2, amino acids 11 to 59 of SEQ ID NO: 2, amino acids 68 to 103 of SEQ ID NO: 2, amino acids 173 to 220 of SEQ ID NO: 2, or amino acids 224 to 319 of SEQ ID NO: 2.

¹ Claims 273-276 and 279-285 were dependent on canceled claim 270 but have been amended to depend from claim 272, which was not rejected by the Examiner. Claim 272 has been rewritten in independent form.

More generally, the claims are directed to isolated polynucleotides comprising a nucleic acid *which encodes a polypeptide* which shares identity to various regions of SEQ ID NO: 2. Applicants disagree with the Examiner that the nucleic acid taught in GenBank Accession No. AA223122 is capable of encoding a contiguous 138 *amino acid* fragment which is 97% identical to the claimed regions of SEQ ID NO: 2 at the polypeptide level.

Assuming a proper reading frame, translation of the nucleic acid taught in GenBank Accession No. AA223122 would result in a polypeptide with a substitution at the amino acid corresponding to position 16 of SEQ ID NO: 2 (Ala to Val) and a substitution at the amino acid corresponding to position 56 (Trp to Leu) of SEQ ID NO: 2. Further, the single nucleotide insertion within GenBank Accession No. AA223122 (which results in a substitution of the amino acid at position 56 of SEQ ID NO: 2 in the corresponding polypeptide) causes a frame shift within the sequences of the down-stream nucleotides. This further results in a non-identical amino acid sequence beginning at the amino acid corresponding to position 56 of SEQ ID NO: 2. In addition, translation of GenBank Accession No. AA223122 results in four stop codons—namely, at positions corresponding to amino acids 58, 69, 72 and 118 of SEQ ID NO: 2. Moreover, any translation of the nucleic acid taught in GenBank Accession No. AA223122 stops at the amino acid corresponding to position 138 of SEQ ID NO: 2 due to the length of the nucleotide sequence. In view of the above, GenBank Accession No. AA223122 does not encode a *contiguous* polypeptide or polypeptide fragment sharing 90%, 95%, or 100% identity with polypeptide fragments comprising amino acids 1-133, 11-59, 68-103, 173-220 or 224-319 of SEQ ID NO: 2. Translation of the nucleic acid sequence in the reference relied upon by the Examiner creates fragments interrupted by termination sequences, completely non-identical fragments (due to the frameshift caused by the nucleotide insertion) or fragments interrupted with non-identical amino acid substitutions within the regions of SEQ ID NO: 2 that are recited in the claims. It is clear then, that GenBank Accession No.

AA223122 does not encode a polypeptide which is 97% identical to the claimed invention over a *contiguous* stretch of amino acids.

To anticipate a claim, the reference must teach every element of the claim. (M.P.E.P. § 2131.) "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Because the reference relied upon by the Examiner does not teach *any* element of the claimed invention, a § 102(a) it cannot anticipate the claims and a rejection is improper. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 225, 226, 230-244, 247-256, 270, 271, and 273-286 under 35 U.S.C. § 103(a) as allegedly being unpatentable over GenBank Accession No. AA223122 and Chinnaiyan *et al.*, *Science* 274: 990-92 (1996), Sibson *et al.*, WO 94/01548, and Bjorn *et al.*, *Current Biol.* 2:569-75 (1992) in view of Adair *et al.*, WO 91/09967. Applicants respectfully disagree.

A finding of obviousness in view of prior art references requires that: (1) the prior art must have suggested to those of ordinary skill in the art that they should make the claimed composition or device or use the claimed method, as the case may be; and (2) the prior art must have revealed that in so doing, those of ordinary skill would have had a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991); *In re O'Farrell*, 853 F.2d 894, 7 U.S.P.Q.2d 1673 (Fed. Cir. 1988); *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). The prior art must provide one of ordinary skill in the art with the motivation to make the modifications required to arrive at the claimed composition. *In re Lalu*, 747 F.2d 703, 705, 223 U.S.P.Q. 1257, 1258 (Fed. Cir. 1984). Finally, in order to render a claim obvious, the prior

art reference (or references when combined) must teach or suggest all the claim limitations.
(M.P.E.P. § 2142.)

The defects of GenBank Accession No. AA223122(V) have been discussed above. Neither Chinnaiyan *et al.*, Sibson *et al.*, Bjorn *et al.* nor Adair *et al.* cure the defects of GenBank Accession No. AA223122 such that an isolated polynucleotide which encodes a contiguous polypeptide within the scope of the claims is taught. As such, the references in combination do not teach every limitation of the claims. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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